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☐	L5	L3 and Staphylococcus	84
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Prev Page Next Page Go to Doc#

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Terms	Documents
L1 and CR1	9

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Terms	Documents
L3 and CR1	3

Prev Page Next Page Go to Doc#

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L5 and anthrax	3

Prev Page Next Page Go to Doc#

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2: Mohamed N, Clagett M, Li J, Jones S, Pincus S, D'Alia G, Nardone L, Babin M, Spitalny G, Casey L. Related Articles, Links

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Items 1 - 19 of 19 One page.

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1: Peng W, Zhang X, Mohamed N, Inghirami G, Takeshita K, Pecora A, Nardone LL, Pincus SE, Casey LS, Spitalny GL. Related Articles, Links

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A transgenic mouse model for studying the clearance of blood-borne pathogens via human complement receptor 1 (CR1).
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Evaluation of antigen-based heteropolymer for treatment of systemic lupus erythematosus in a nonhuman primate model.

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TITLE: Mammalian primate erythrocyte bound heteropolymerized monoclonal antibodies and methods of use thereof

DATE-ISSUED: January 30, 1996

INVENTOR-INFORMATION:

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US-CL-CURRENT: 424/136.1; 424/142.1, 424/147.1, 424/150.1, 424/153.1, 435/70.21, 530/387.3, 530/388.15, 530/388.3, 530/388.4

CLAIMS:

What is claimed is:

1. A method of therapeutically treating a primate individual with a target antigen present in its circulatory system, said target antigen being selected from the group consisting of a virus, a microorganism and a protein, comprising administering to said individual a therapeutically effective amount of a monoclonal antibody heteropolymer comprising a first monoclonal antibody specific for CR1 receptor cites on the surface of erythrocytes of said individual, said first monoclonal antibody being cross-linked to a second monoclonal antibody specific for said target antigen.

2. The method of claim 1, wherein said monoclonal antibodies are obtained from a non-human host.

3. The method of claim 1, wherein said antibodies are obtained from a human host.

4. The method of claim 1, wherein said antigen is a virus.

5. The method of claim 1, wherein said antigen is a microorganism.

6. The method of claim 1, wherein said antigen is a protein.

1: Cancer Immunol Immunother. 1997 Nov-Dec;45(3-4):152-5.

Clearance of blood-borne pathogens mediated through bispecific monoclonal antibodies bound to the primate erythrocyte complement receptor.

Taylor RP, **Nardin A**, **Sutherland WM**.

Department of Biochemistry, University of Virginia School of Medicine, Charlottesville 22908, USA.

The primate erythrocyte complement receptor facilitates both the immune adherence reaction and the immune complex clearance properties of primate erythrocytes. These phenomena have been studied for more than 40 years. However, it has only recently become apparent that these characteristics of primate erythrocytes may be useful in the generation of a therapy based on bispecific monoclonal antibodies. Our approach uses bispecific monoclonal antibody constructs (heteropolymers) that promote binding of specific target pathogens to primate erythrocytes via the complement receptor. Once bound to the erythrocytes, the pathogen-heteropolymer complex should be cleared from the circulation, phagocytosed and destroyed in the liver. Results with several prototype target pathogens in monkey models indicate it may be possible to use this technology to develop a robust and general therapy for the treatment of diseases associated with blood-borne pathogens.

PMID: 9435861 [PubMed - indexed for MEDLINE]

1: J Hematother. 1995 Oct;4(5):357-62.

Links

Primate erythrocyte (E) complement receptor (CR1) as an anchor site for bispecific-based therapies to clear pathogens or autoantibodies safely from the circulation.

Taylor RP, Ferguson PJ.

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We have prepared cross-linked, bispecific complexes [heteropolymers (HP) and antigen-based heteropolymers (AHP)] that facilitate complement-independent binding of target model pathogens or autoantibodies to primate erythrocytes (E) via complement receptors (CR1). The method is based on using monoclonal antibodies (mAb) specific for CR1 that either are cross-linked to an mAb specific for a prototype pathogen (e.g., IgE) or are cross-linked to an autoantigen (e.g., dsDNA) that is recognized by circulating pathogenic autoantibodies in the autoimmune disease systemic lupus erythematosus (SLE). The underlying assumption in this research is that complexed ligands containing IgG bound to primate E CR1 should be recognized and processed via the same mechanism by which complement-opsonized immune complexes bound to E CR1 are cleared from the circulation and phagocytosed in the liver and spleen. Our work in experimental monkey models has demonstrated that binding of substrates to primate E via this method does indeed lead to the safe and rapid clearance of the target pathogens or autoantibodies from the circulation, without any lysis or loss of the E. Although a number of questions must still be resolved, it may be possible to generalize these findings and use this CR1-based approach to develop a simple noninvasive bispecific therapy that can be used to clear pathogens or autoantibodies from the circulation.

PMID: 8581369 [PubMed - indexed for MEDLINE]